Abstract No. bert683

Crystal Structure of the Type III Secretion Chaperone SigE

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Beamline(s): X12C

Introduction: Several gram negative bacterial pathogens have evolved a type III secretion system to deliver virulence effector proteins directly into eukaryotic cells, a process essential for disease [1]. This specialized secretion process requires customized chaperones that are specific for particular effector proteins. Despite the low sequence similarities, most type III secretion chaperones are small (<20 kDa), acidic and dimeric. The crystal structure of the *Salmonella typhimurium* SigD-specific chaperone has been determined at 1.9 Å resolution [2].

Methods and Materials: The crystal structure of intact SigE was solved by MAD phasing using a seleno-methionine derivative [3]. All data was collected at 100 K in a cryogenic stream. Three-wavelengths data was collected at the Se absorption peak, edge and high energy remote.

Results: The crystal structure of SigE reveals a novel fold with a-b-b-b-a-b-b-a topology (Fig. 1a). This topology differs significantly from that of SecB, the type II general secretory chaperone [4]. As expected from its acidic pI, SigE has a significant level of negatively charged electrostatic surface area; the charged surface is relatively localized to one face of the molecule and is interspersed with exposed hydrophobic surface (Fig. 1c).
Previous work supports the existence of a dimeric form of SigE, *in vivo* and *in vitro*. Accordingly, the asymmetric unit of the SigE crystals contains a homo-dimer in which the two monomers are related by an approximate 2-fold non-crystallographic rotation symmetry. The dimerization interface arises through symmetrical interactions between the region containing the helix-strand motif, a2-b4, and its dimeric counterpart (a'1-b'4) in such a way that a2 and a'2 are approximately parallel (Fig. 1b). The buried area between the dimeric interface is ~2190 Å, predominantly hydrophobic with additional hydrogen bonded interactions by polar side chains.

Acknowledgments: Work in our laboratory was supported by the Burroughs Welcome Foundation, the Howard Hughes Medical Research Institute, Canadian Institute of Health Research, the Canadian Bacterial Disease Network Center of Excellence and the Toronto Hospital for Sick Children. We are thankful to excellent technical support at the beamline X12C at NSLS.

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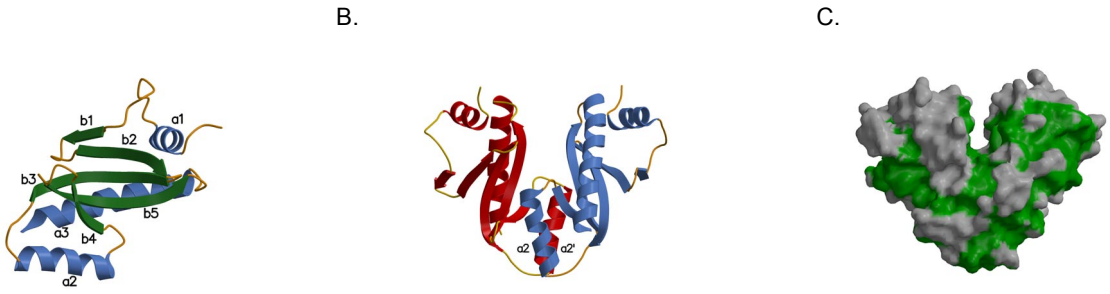

Figure 1. Structure of SigE. A. Ribbon diagram of SigE monomer. B. Ribbon diagram of SigE dimer. C. Surface of SigE (hydrophobic surface in green).